REMARKS

Claims 1-3, 8, 10, and 11 have been amended and claim 57 has been added. Claims 9, 12-44, and 46-56 have been canceled without prejudice or disclaimer. Claims 1-8, 10, 11, 45, and 57 are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 13, lines 6-12; page 15, lines 19-22 and lines 29-31; page 20, line 27 to page 21, line 2; page 23, lines 16-19; page 27, lines 6-17; and page 33, lines 22-28; and Figures 1A-1C; 2A-2D; and 3A-3C. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Rejections of claims 1-8, 10, 11, and 45 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1, 2, 4-8, 10, 11, and 45 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that because ATCC Deposit No. PTA-964 does not appear to be publicly available or capable of being reproducibly isolated from nature without undue experimentation, and the claims require the use of this deposit, the mere reference to the deposit in the specification is insufficient to ensure that all of the conditions of 37 C.F.R. §§ 1.803-1.809 have been met. The Action also states that a deposit made in full compliance with 37 C.F.R. §§ 1.803-1.809 would satisfy the requirements of 35 U.S.C. § 112, first paragraph, provided that Applicants submit a statement by an attorney of record over his or her signature, stating that a deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. The Action further states that the instant specification must be amended to recite the date of the deposit and the complete name and address of the depository, and that the claims must be amended to recite the accession number.

Pursuant to the Examiner's request, Applicants' representative submits the following statement: Applicants deposited cDNA, subcloned into pSPORT1, encoding human CHL polypeptide with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209. The deposit was accepted by the ATCC, an International Depository

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Authority, under the provisions of the Budapest Treaty, and the deposit was designated as PTA-964. A copy of the ATCC receipt for this deposit, showing the patent deposit designation (Accession No. PTA-964) and the date on which the deposit was received by the ATCC (November 16, 1999) is attached. Pursuant to 37 C.F.R. § 1.808(a)(2), the deposit was made under conditions that assure that all restrictions imposed by the depositors on the availability to the public of the deposited material would be irrevocably removed upon the granting of a patent relying on the deposited biological material. In making the deposit, Applicants acknowledged their responsibility, pursuant to 37 C.F.R. § 1.805, to provide a replacement or supplemental deposit if the depository possessing the deposit is unable to furnish samples thereof or is able to furnish samples thereof but the deposit has become contaminated or has lost its capability to function as described in the specification. With regard to the assertion that the date of the deposit and the complete name and address of the depository is not referred to in the body of the specification, Applicants respectfully direct the Examiner's attention to page 92, lines 23-27 of the as-filed specification, where Applicants disclose that a deposit of cDNA encoding human CHL polypeptide, subcloned into the pSPORT1 vector, and having Accession No. PTA-964, was made with the American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209 on November 16, 1999. With regard to the assertion that the accession number of the deposit is not referred to in the claims, Applicants respectfully direct the Examiner's attention to claims 1(b) and 2(b)-2(d), as originally filed. Applicants contend that all the requirements of 37 C.F.R. §§ 1.801-1.809 have been met. *In re Lundak,* 225 U.S.P.Q. 90 (Fed. Cir. 1985). Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 1-8, 10, 11, and 45 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that because the claims do not require that the claimed nucleic acid molecules encode polypeptides possessing any particular activity, and the recitation of the phrase "has an activity of the polypeptide set forth in . . . SEQ ID NO: 8" does not lead one of ordinary skill in the art to a particular activity, the claims are directed to a genus of nucleic acid molecules that is defined only by some level of nucleotide sequence similarity. The Action also states that because the claims do not place any limit on the number of nucleotide substitutions, deletions, insertions, or additions that may be made to the CHL

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molecules of the invention, the claimed genus of nucleic acid molecules is highly variant. The Action asserts that because the genus of nucleic acid molecules encompassed by the claims is highly variant, the specification does not contain a sufficient recitation of the common attributes or characteristics that identify members of the genus, and one of ordinary skill in the art cannot envision the detailed structure of the genus, the specification does not meet the written description requirement for claiming such a genus.

Applicants respectfully disagree with the Action's assertion that the recitation of the phrase "has an activity of the polypeptide set forth in . . . SEQ ID NO: 8" does not lead one of ordinary skill in the art to a particular activity for the CHL polypeptides encoded by the nucleic acid molecules of the invention, and therefore, that the claims are directed to a genus of nucleic acid molecules that is defined only by some level of nucleotide sequence similarity. Applicants contend, instead, that in view of the teachings in the instant specification, one of ordinary skill in the art would readily recognize the specific activities possessed by CHL polypeptides. Applicants note, for example, that the instant specification teaches that CHL polypeptides, like chordin, are capable of antagonizing an endogenous ventralizing factor (likely to be BMP4) in *Xenopus* embryos (Example 9); that CHL polypeptides, like chordin, are capable of inhibiting BMP4 activity (Example 10); that CHL polypeptides co-immunoprecipitate with BMP4, and therefore, that CHL polypeptides, like chordin, directly interact with BMP4 (Example 11); and that CHL polypeptides mediate BMP4-dependent cell proliferation in A5-F cells (Example 12). In view of the teachings in the instant specification regarding the specific activities of CHL polypeptides, Applicants contend, therefore, that the claims are *not* directed to a genus of nucleic acid molecules that is defined *only* by some level of nucleotide sequence similarity, but rather are directed to nucleic acid molecules encoding polypeptides possessing one of these specific activities.

Applicants also respectfully disagree with the Action's assertion that the claims do not place any limit on the number of nucleotide substitutions, deletions, insertions, or additions that may be made to the CHL molecules of the invention, and therefore, that the claimed genus of nucleic acid molecules is highly variant. Applicants note that claim 1 has been amended to recite an isolated nucleic acid molecule comprising a nucleotide sequence as set forth in SEQ ID NO: 7; a nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-964; a nucleotide sequence encoding the polypeptide of SEQ ID NO: 8; or a nucleotide sequence that is complementary to any of these

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nucleotide sequences. Applicants also note that claim 1, as amended, no longer recites an isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes under moderately or highly stringent conditions to the complement of any of the nucleotide sequences recited in claims 1(a)-(c).

Applicants contend that the genus of molecules encompassed by amended claim 1 is not highly variant, as this claim does not encompass nucleic acid molecules encoding CHL polypeptides containing any number of substitutions, deletions, insertions, or additions, and that one of ordinary skill in the art could readily determine the structure of the nucleic acid molecules falling within the scope of this claim with reference to the explicitly-disclosed sequence and their deposit. *Enzo Biochem Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316 (Fed. Cir. 2002). Applicants, therefore, submit that amended claim 1 satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection of this claim on this ground be withdrawn.

In addition, Applicants note that claim 2 has been amended to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 8, wherein the residue at position 95 is glutamic acid and the residues at positions 319-323 are glycine-lysine-lysine-alanine-lysine, and wherein the encoded polypeptide has an activity of the polypeptide of SEQ ID NO: 8; a region of the nucleotide sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 encoding a polypeptide fragment of SEQ ID NO: 8 of at least 377 residues; a region of the nucleotide sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 comprising a fragment of at least 1131 nucleotides; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants also note that claim 2, as amended, no longer recites an isolated nucleic acid molecule comprising a nucleotide sequence encoding an allelic or splice variant of the nucleotide sequence of SEQ ID NO: 7, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-964, or the nucleotide sequence recited in claim 2(a); or a nucleotide sequence that hybridizes under moderately or highly stringent conditions to the complement of any of the nucleotide sequences recited in claims 2(a)-(d).

Applicants contend that the genus of molecules encompassed by amended claim 2 is not highly variant, as this claim does not encompass nucleic acid molecules encoding CHL polypeptides containing any number of substitutions, deletions, insertions, or additions. With regard to the genus of nucleic acid molecules defined by amended claim 2(a), Applicants contend that the number of

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nucleotide substitutions is limited by the requirement that the polypeptide encoded by a particular nucleic acid molecule have an activity of the polypeptide of SEQ ID NO: 8. As discussed above, Applicants contend that in view of the teachings in the instant specification, one of ordinary skill in the art would readily recognize the specific activities possessed by CHL polypeptides. With regard to the genus of nucleic acid molecules defined by amended claim 2(b) and (c), Applicants contend that because the specification explicitly teaches the nucleotide and amino acid sequences for human CHL polypeptide (Figures 3A-3C), the specification inherently discloses fragments of human CHL polypeptide, since fragments are merely portions of the specifically disclosed full-length human CHL polypeptide sequence. Applicants, therefore, contend that the genus of molecules encompassed by amended claim 2 is not highly variant, and that one of ordinary skill in the art could readily determine the structure of nucleic acid molecules falling within the scope of this claim. Applicants, therefore, submit that amended claim 2 satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection of this claim on this ground be withdrawn.

Finally, Applicants note that claim 3 has been amended to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 8; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 having a C- and/or N-terminal truncation, wherein the encoded polypeptide comprises at least 377 amino acid residues; a portion of the first nucleotide sequence comprising a fragment of at least 1131 residues; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants also note that claim 3, as amended, no longer recites an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide of SEQ ID NO: 8 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide of SEQ ID NO: 8; a nucleotide sequence encoding a polypeptide of SEQ ID NO: 8 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide of SEQ ID NO: 8; or a nucleotide sequence that hybridizes under moderately or highly stringent conditions to the complement of any of the nucleotide sequences recited in claims 3(a)-(f).

Applicants contend that the genus of molecules encompassed by amended claim 3 is not highly variant, as this claim does not encompass nucleic acid molecules encoding CHL polypeptides

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containing any number of substitutions, deletions, insertions, or additions. With regard to the genus of nucleic acid molecules defined by amended claim 3(a), Applicants contend that the number of amino acid substitutions is limited by the requirement that the polypeptide encoded by a particular nucleic acid molecule have an activity of the polypeptide of SEQ ID NO: 8. As discussed above, Applicants contend that in view of the teachings in the instant specification, one of ordinary skill in the art would readily recognize the specific activities possessed by CHL polypeptides. Moreover, Applicants note that the instant application teaches the amino acid sequences for murine, rat, and human FGF-like polypeptide (Figures 1A-1C, 2A-2D, and 3A-3C); that conservative amino acid substitutions may be made in those portions of human CHL polypeptide that are not conserved among CHL orthologs (page 27, lines 6-17); and rubrics recognized in the art for making conservative amino acid substitutions (Table I; pages 26-27). Applicants also contend that because the specification explicitly teaches the amino acid sequences for murine, rat, and human CHL polypeptide and that conservative amino acid substitutions may be made in those portions of human CHL polypeptide that are not conserved among CHL orthologs, the specification implicitly discloses those positions within human CHL polypeptide that are tolerable of conservative substitution. With regard to the genus of nucleic acid molecules defined by amended claim 3(b), Applicants contend that because the specification explicitly teaches the nucleotide and amino acid sequences for human CHL polypeptide (Figures 3A-3C), the specification inherently discloses truncations of human CHL polypeptide, since truncated CHL polypeptides are merely portions of the specifically disclosed full-length human CHL polypeptide sequence. Applicants, therefore, contend that the genus of molecules encompassed by amended claim 3 is not highly variant, and that one of ordinary skill in the art could readily determine the structure of nucleic acid molecules falling within the scope of this claim. Applicants, therefore, submit that amended claim 3 satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection of this claim on this ground be withdrawn.

The Office Action also asserts a rejection of claims 1-8, 10, 11, and 45 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that in view of the breadth of the claims and lack of sufficient guidance in the specification regarding the positions of CHL polypeptide that are

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essential for its biological activity, one of ordinary skill in the art would be left to extensive trial and error experimentation in order to identify nucleic acid molecules that encode polypeptides which retain CHL polypeptide function, and therefore, would require undue experimentation to make and use the full scope of the claimed invention.

As described above, Applicants have amended claims 1-3 so that they no longer recite an isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes under moderately or highly stringent conditions to the complement of any of the nucleotide sequences recited in claims 1(a)-(c); a nucleotide sequence encoding an allelic or splice variant of the nucleotide sequence of SEQ ID NO: 7, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-964, or the nucleotide sequence recited in claim 2(a); a nucleotide sequence that hybridizes under moderately or highly stringent conditions to the complement of any of the nucleotide sequences recited in claims 2(a)-(d); a nucleotide sequence encoding a polypeptide of SEQ ID NO: 8 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide of SEQ ID NO: 8; a nucleotide sequence encoding a polypeptide of SEQ ID NO: 8 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide of SEQ ID NO: 8; or a nucleotide sequence that hybridizes under moderately or highly stringent conditions to the complement of any of the nucleotide sequences recited in claims 3(a)-(f). Applicants contend that the claims, as amended, are not overly broad. Applicants further contend that the explicit teachings, combined with knowledge well-known in the art, would permit one of ordinary skill in the art to make and use the claimed invention throughout its full scope without the exercise of undue experimentation. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

2. Rejections of claims 1-8, 10, 11, and 45 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, and 45 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

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The Action first asserts that claims 1-8, 10, 11, and 45 are indefinite for the recitation in claims 1-3 of the phrase "moderately or highly stringent conditions," because the specification fails to precisely define "moderately or highly stringent conditions."

Applicants note that claims 1-3, as amended, no longer recite the phrase "moderately or highly stringent conditions," thereby rendering this ground of rejection moot.

The Action next asserts that claims 8 and 10 are indefinite for reciting the term "CHL polypeptide," because the specification does not identify the material element or combination of elements that is definitive of a "CHL polypeptide," and therefore, a skilled artisan would be unable to determine what additional or material limitations are placed upon a claim by the presence of this element.

Applicants respectfully disagree with the Action's assertion that claims 8 and 10 are indefinite for reciting the term "CHL polypeptide." Applicants note that an explicit definition of the term "CHL polypeptide" is provided in the specification at page 15, lines 10-18, and contend that this definition controls the interpretation of the term as it is used in the claims of the instant application. Applicants contend, for example, that it would be apparent to one of ordinary skill in the art that a polypeptide comprising the amino acid sequence of SEQ ID NO: 8 is a CHL polypeptide. Applicants further contend that it would be apparent to one of ordinary skill in the art that a polypeptide variant of the amino acid sequence of SEQ ID NO: 8 is a CHL polypeptide. However, in order to expedite prosecution of the pending claims to allowance, and in Applicants' view because it will have no substantive effect in the proper scope of the pending claims, Applicants have amended claim 8 to recite a process of producing a polypeptide encoded by the nucleic acid molecule of any of Claims 1, 2, or 3, and have amended claim 10 to recite that the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native CHL gene operatively linked to the nucleic acid molecule. Applicants note that an explicit definition of the term "CHL gene" is provided in the specification at page 13, lines 6-12. Applicants contend, therefore, that claims 8 and 10, as amended, are not indefinite, and respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 2-8, 10, 11, and 45 are indefinite for the recitation in claims 2 and 3 of the phrase "has an activity of the polypeptide set forth in . . . SEQ ID NO: 8," because the specification does not identify the material element or combination of elements that is

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definitive of an "an activity of the polypeptide set forth in . . . SEQ ID NO: 8," and therefore, a skilled artisan would be unable to determine what additional or material limitations are placed upon a claim by the presence of this element.

Applicants respectfully disagree with the Action's assertion that claims 2 and 3 are indefinite for reciting the phrase "has an activity of the polypeptide set forth in . . . SEQ ID NO: 8." Applicants note that the instant specification teaches several specific activities possessed by CHL polypeptides. For example, the instant specification teaches that CHL polypeptides, like chordin, are capable of antagonizing an endogenous ventralizing factor (likely to be BMP4) in *Xenopus* embryos (Example 9); that CHL polypeptides, like chordin, are capable of inhibiting BMP4 activity (Example 10); that CHL polypeptides co-immunoprecipitate with BMP4, and therefore, that CHL polypeptides, like chordin, directly interact with BMP4 (Example 11); and that CHL polypeptides mediate BMP4-dependent cell proliferation in A5-F cells (Example 12). The instant specification also teaches that BMP4 plays a role in the regulation of bone-mass (page 86, lines13-14) and in organ formation in the embryonic kidney, lung, and gut (page 87, lines 3-5), and therefore, that CHL polypeptides and anti-CHL antibodies can be used to modulate BMP4 activity (page 86, lines 21-24 and page 87, lines 7-11). In view of the teachings in the instant specification regarding the specific activities of CHL polypeptides, Applicants contend that one of ordinary skill in the art would understand the meaning of the phrase "has an activity of the polypeptide set forth in . . . SEQ ID NO: 8." Applicants, therefore, contend that the phrase "has an activity of the polypeptide set forth in . . . SEQ ID NO: 8" is not indefinite, and respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 1-8, 10, 11, and 45 are indefinite for the recitation in claims 1-3 of the term "complementary to," because it is unclear whether the claimed nucleic acid molecule is a full length complement of a recited nucleic acid molecule or complementary only to some portion of the recited nucleic acid molecule.

Applicants respectfully disagree with the Action's assertion that claims 1-3 are indefinite for reciting the term "complementary to." Applicants contend that the nucleotide sequence complement of the nucleotide sequence 5'-A-G-C-T-A-G-C-T-3', for example, is well understood in the art to be 5'-T-C-G-A-T-C-G-A-3', rather than the nucleotide sequence 5'-T-C-G-3' or some other portion of the nucleotide sequence 5'-T-C-G-A-T-C-G-A-3'. Applicants contend, therefore, that one of ordinary skill in the art would understand that a nucleotide sequence that is complementary to, for

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example, the coding portion of the nucleotide sequence of SEQ ID NO: 7 must be *the same length* as that portion of the nucleotide sequence of SEQ ID NO: 7 (*i.e.*, 1359 nucleotides). Moreover, Applicants contend that such a meaning is consistent with the meaning of the term in the art. For example, the term "complementary to" is given the meaning "a mold of the original," such that the sequence of nucleotides in a nucleic acid molecule is *preserved* in its complementary strand by Alberts *et al.* (*Molecular Biology of the Cell*, pp. 5-7 (Garland Publishing, Inc., 1994)). Applicants, therefore, respectfully contend that claims 1-3, as amended, fulfill the requirements of 35 U.S.C. § 112, first paragraph.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

3. Rejection of claims 1-8, 10, 11, and 45 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1-5, 7, and 11 under 35 U.S.C. § 102(a), as being anticipated by GenBank Accession No. AI246227, published January 28, 1999, which discloses the nucleotide sequence of the cDNA insert of I.M.A.G.E. Consortium clone 1857913, which was made available to the public on December 14, 1998. The Action states that because this reference discloses a nucleotide sequence that is 99.7% identical to nucleotides 734-1088 of the nucleotide sequence of SEQ ID NO: 7, and the metes and bounds of the terms "complementary" and "has an activity of the polypeptide set forth in . . . SEQ ID NO: 8" are not clearly set forth, the disclosed nucleotide sequence is encompassed by claims 1(d), 1(e), 2(c)-(f), 3(c), 3(b), and 3(f)-(h). The Action further states that because nucleic acid molecule disclosed by NCI-CGAP was cloned, I.M.A.G.E. Consortium clone 1857913 discloses a vector and prokaryotic host comprising the disclosed nucleic acid molecule.

Applicants note that GenBank Accession No. AI246227 discloses a nucleic acid molecule of 355 nucleotides that encodes a 117 amino acid fragment of the polypeptide of SEQ ID NO: 8. The instant application teaches a nucleic acid molecule of 1496 nucleotides (SEQ ID NO: 7) that comprises an open reading frame of 1359 nucleotides that encodes a human CHL polypeptide of 452 amino acids (SEQ ID NO: 8). As described in section 1 above, Applicants have amended claim 1 to recite an isolated nucleic acid molecule comprising a nucleotide sequence as set forth in SEQ ID NO:

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7; a nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-964; a nucleotide sequence encoding the polypeptide of SEQ ID NO: 8; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because GenBank Accession No. AI246227 discloses a nucleotide sequence of 355 nucleotides encoding a polypeptide of 117 amino acids, the disclosed sequence is not encompassed by the genus of nucleotide sequences defined by claim 1, and therefore, this reference cannot anticipate claim 1.

As also described in section 1 above, Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 8, wherein the residue at position 95 is glutamic acid and the residues at positions 319-323 are glycine-lysine-lysine-alanine-lysine, and wherein the encoded polypeptide has an activity of the polypeptide of SEQ ID NO: 8; a region of the nucleotide sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 encoding a polypeptide fragment of SEQ ID NO: 8 of at least 377 residues; a region of the nucleotide sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 comprising a fragment of at least 1131 nucleotides; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because GenBank Accession No. AI246227 discloses a nucleotide sequence of 355 nucleotides encoding a polypeptide of 117 amino acids, the disclosed sequence is not encompassed by the genus of nucleotide sequences defined by claim 2, and therefore, this reference cannot anticipate claim 2.

As also described in section 1 above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 8; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 having a C- and/or N-terminal truncation, wherein the encoded polypeptide comprises at least 377 amino acid residues; a portion of the first nucleotide sequence comprising a fragment of at least 1131 residues; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because GenBank Accession No. AI246227 discloses a nucleotide sequence of 355 nucleotides encoding a polypeptide of 117 amino acids, the disclosed sequence is not encompassed by the genus of nucleotide sequences defined by claim 3, and therefore, this reference cannot anticipate claim 3.

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Because GenBank Accession No. AI246227 does not disclose a nucleotide sequence that meets each and every limitation of the claimed invention, this reference cannot anticipate claims 1-5, 7, and 11, as amended. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 1-5, 7, 11, and 45 under 35 U.S.C. § 102(a), as being anticipated by International Publication No. WO 99/57132 (the '132 publication), published November 11, 1999. The Action states that because this reference discloses a nucleotide sequence that is 99.7% identical to nucleotides 44-1495 of the nucleotide sequence of SEQ ID NO: 7, the disclosed nucleotide sequence encodes a polypeptide that is 99.8% identical to the polypeptide of SEQ ID NO: 8, and the metes and bounds of the terms "has an activity of the polypeptide set forth in . . . SEQ ID NO: 8" and "CHL polypeptide" are not clearly set forth, the disclosed nucleotide sequence is encompassed by claims 1(d), 1(e), 2(a)-(f), and 3(a)-(h). The Action further states that the '132 publication discloses vectors comprising the disclosed nucleic acid molecule, the disclosed nucleic acid molecule linked to expression control sequences, transformed host cells comprising the disclosed nucleic acid molecule, and recombinant methods for producing the polypeptide encoded by the disclosed nucleic acid molecule.

Applicants note that the '132 publication discloses a nucleic acid molecule of 3861 nucleotides encoding a polypeptide of 457 amino acids. Applicants also note that the polypeptide of SEQ ID NO: 8 differs from the polypeptide disclosed in the '132 publication in that, *inter alia*, the glutamic acid residue at position 95 of SEQ ID NO: 8 is deleted in the polypeptide disclosed in the '132 publication. As described above, Applicants have amended claim 1 to recite an isolated nucleic acid molecule comprising a nucleotide sequence as set forth in SEQ ID NO: 7; a nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-964; a nucleotide sequence encoding the polypeptide of SEQ ID NO: 8; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because the nucleic acid molecule disclosed in the '132 publication encodes a polypeptide that has a single amino acid deletion at position 95 of SEQ ID NO: 8, the disclosed sequence is not encompassed by the genus of nucleotide sequences defined by claim 1, and therefore, this reference cannot anticipate claim 1.

As also described above, Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that is at least 70 percent

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identical to the polypeptide set forth in SEQ ID NO: 8, wherein the residue at position 95 is glutamic acid and the residues at positions 319-323 are glycine-lysine-lysine-alanine-lysine, and wherein the encoded polypeptide has an activity of the polypeptide of SEQ ID NO: 8; a region of the nucleotide sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 encoding a polypeptide fragment of SEQ ID NO: 8 of at least 377 residues; a region of the nucleotide sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 comprising a fragment of at least 1131 nucleotides; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because the nucleic acid molecule disclosed in the '132 publication encodes a polypeptide that lacks a glutamic acid residue at position 95 of SEQ ID NO: 8, does not encode a polypeptide fragment of SEQ ID NO: 8 of at least 377 residues, and does not comprise a region of the nucleotide sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 comprising a fragment of at least 1131 nucleotides, the disclosed sequence is not encompassed by the genus of nucleotide sequences defined by claim 2, and therefore, this reference cannot anticipate claim 2.

As also described above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 8; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 having a C- and/or N-terminal truncation, wherein the encoded polypeptide comprises at least 377 amino acid residues; a portion of the first nucleotide sequence comprising a fragment of at least 1131 residues; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because one of ordinary skill in the art could not generate the polypeptide disclosed in the '132 publication by making *only* conservative substitutions in the polypeptide of SEQ ID NO: 8, the disclosed sequence is not encompassed by the genus of nucleotide sequences defined by claim 3(a). Applicants also contend that because the nucleic acid molecule disclosed in the '132 publication does not encode a polypeptide fragment of SEQ ID NO: 8 of at least 377 residues, and does not comprise a region of a conservatively substituted polypeptide of SEQ ID NO: 8 comprising a fragment of at least 1131 nucleotides, the disclosed sequence is not encompassed by the genus of nucleotide sequences defined by claim 3(b) or (d). Applicants, therefore, contend that this reference cannot anticipate claim 3.

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Because the '132 publication does not disclose a nucleotide sequence that meets each and every limitation of the claimed invention, this reference cannot anticipate claims 1-5, 7, 11, and 45, as amended. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 3-8, 10, and 45 under 35 U.S.C. § 102(b), as being anticipated by U.S. Patent No. 5,693,775 (the '775 patent), which issued to Nathans *et al.* on December 2, 1997. The Action states that because claim 3(e)-(h) encompasses essentially any and all polypeptides, the '775 patent discloses a nucleic acid molecule that is encompassed by claim 3(e)-(h). The Action also states that the '775 patent discloses a vector comprising the disclosed nucleic acid molecule, eukaryotic and prokaryotic host cells comprising the vector, and methods of making the polypeptide encoded by the disclosed nucleic acid molecule.

Applicants respectfully disagree with the Action's assertion that the '775 Patent, which discloses the nucleotide and amino acid sequences of a molecule that is completely unrelated to CHL polypeptide – specifically, fibroblast growth factor homologous factor-1 – could anticipate claims directed to nucleic acid sequences encoding CHL polypeptides and CHL polypeptide variants. Nevertheless, as described in section 1 above, Applicants have amended claim 3(c), (d), and (e) (formerly claim 3(e), (f), and (h)) to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 8, and/or having a C- and/or N-terminal truncation, wherein the encoded polypeptide comprises at least 377 amino acid residues; a portion of a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 8, and wherein the nucleotide sequence comprises a fragment of at least 1131 residues; or a nucleotide sequence that is complementary to any of these nucleotide sequences, and have amended claim 3 to delete originally-filed claim 3(g). Applicants contend that because amended claim 3 does not encompass essentially any and all polypeptides (*e.g.*, amended claim 3 does not encompass the nucleic acid molecules disclosed by either GenBank Accession No. AI246227 or the '132 publication), the nucleotide sequence disclosed by Nathans *et al.* cannot anticipate claims 3-8, 10, and 45. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 1-8, 10, and 45 under 35 U.S.C. § 102(a),

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as being anticipated by International Publication No. WO 98/40483 (the '483 publication), published September 17, 1998. The Action states that because this reference discloses a first nucleotide sequence that is 98.7% identical to the nucleotide sequence of SEQ ID NO: 7, which encodes a polypeptide that is identical to residues 21-318 of the polypeptide of SEQ ID NO: 8, and a second nucleotide sequence that is 98% identical to the nucleotide sequence of SEQ ID NO: 7, and which encodes a polypeptide that is identical to residues 157-318 of the polypeptide of SEQ ID NO: 8, the disclosed nucleotide sequences are encompassed by claims 1(d), 1(e), 2(a)-(f), and 3(a)-(h). The Action further states that the '483 publication discloses vectors and host cells comprising the disclosed nucleic acid molecules and recombinant methods for producing the polypeptides encoded by the disclosed nucleic acid molecules.

Applicants note that the '483 publication discloses (1) a nucleic acid molecule of 1732 nucleotides that encodes a polypeptide of 305 amino acids, and (2) a nucleic acid molecule of 2315 nucleotides that encodes a polypeptide of 464 amino acids. Applicants also note that the polypeptide of SEQ ID NO: 8 differs from the both polypeptides disclosed in the '483 publication in that, *inter alia*, the glycine-lysine-lysine-alanine-lysine residues at positions 319-323 of SEQ ID NO: 8 are deleted in the polypeptides disclosed in the '483 publication. As described above, Applicants have amended claim 1 to recite an isolated nucleic acid molecule comprising a nucleotide sequence as set forth in SEQ ID NO: 7; a nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-964; a nucleotide sequence encoding the polypeptide of SEQ ID NO: 8; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because the nucleic acid molecules disclosed in the '483 publication encode polypeptides that have an amino acid deletion at positions 319-323 of SEQ ID NO: 8 (and one of the polypeptides disclosed in the '483 publication is only 305 amino acids in length), the disclosed sequences are not encompassed by the genus of nucleotide sequences defined by claim 1, and therefore, this reference cannot anticipate claim 1.

As also described above, Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 8, wherein the residue at position 95 is glutamic acid and the residues at positions 319-323 are glycine-lysine-lysine-alanine-lysine, and wherein the encoded polypeptide has an activity of the polypeptide of SEQ ID NO: 8; a region of the nucleotide

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sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 encoding a polypeptide fragment of SEQ ID NO: 8 of at least 377 residues; a region of the nucleotide sequence of SEQ ID NO: 7 or the DNA insert in ATCC Deposit No. PTA-964 comprising a fragment of at least 1131 nucleotides; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because the nucleic acid molecules disclosed in the '483 publication encode polypeptides that have an amino acid deletion at positions 319-323 of SEQ ID NO: 8 (and one of the polypeptides disclosed in the '483 publication is only 305 amino acids in length), the disclosed sequences are not encompassed by the genus of nucleotide sequences defined by claim 2, and therefore, this reference cannot anticipate claim 2.

As also described above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 8; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 having a C- and/or N-terminal truncation, wherein the encoded polypeptide comprises at least 377 amino acid residues; a portion of the first nucleotide sequence comprising a fragment of at least 1131 residues; or a nucleotide sequence that is complementary to any of these nucleotide sequences. Applicants contend that because one of ordinary skill in the art could not generate either of the polypeptides disclosed in the '483 publication by making *only* conservative substitutions in the polypeptide of SEQ ID NO: 8, the disclosed sequences are not encompassed by the genus of nucleotide sequences defined by claim 3(a). Applicants also contend that because both of the nucleic acid molecules disclosed in the '483 publication do not encode polypeptide fragments of SEQ ID NO: 8 of at least 377 residues, and do not comprise a region of a conservatively substituted polypeptide of SEQ ID NO: 8 comprising a fragment of at least 1131 nucleotides, the disclosed sequences are not encompassed by the genus of nucleotide sequences defined by claim 3(b) or (d). Applicants, therefore, contend that this reference cannot anticipate claim 3.

Because the '483 publication does not disclose a nucleotide sequence that meets each and every limitation of the claimed invention, this reference cannot anticipate claims 1-8, 10, and 45, as amended. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

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Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

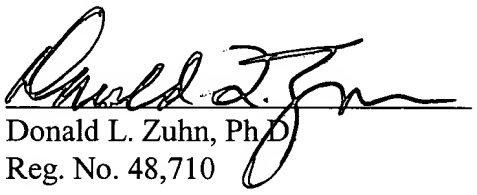
CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Romeo believes it to be helpful, he is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: September 19, 2003

By: 
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